GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION
SPONSORED PROJECT INITIATION

Date: 9/18/78

Project Title: Hemodynamics of Normal and Diseased Carotid Arteries

Project No: E-16-D01

Project Director: Dr. D. P. Giddens

Sponsor: DHEW/PHS/National Heart, Lung and Blood Institute

Agreement Period: From 9/1/78 Until 8/31/79 (01 year)

Type Agreement: Grant No. 1 R01 H122635-01

Amount: $74,382 (PHS - E-16-D01)
3,915 (GIT - E-16-331)
$78,297 TOTAL

Reports Required: Interim Reports, Terminal Progress Report

Sponsor Contact Person (s):

Technical Matters

Don H. Blount, Ph. D.
Acting Assoc. Dir. for Cardiology
Division of Heart & Vascular Diseases
Nat'l. Heart, Lung & Blood Institute
National Institute of Health
Bethesda, Maryland 20014

Contractual Matters
(thru OCA)

James M. Pike, Chief
Grants Operation Branch
Division of Extramural Affairs
Nat'l. Heart, Lung & Blood Institute
National Institute of Health
Bethesda, MD 20014

Defense Priority Rating: N/A

Assigned to: Aerospace Engineering (School/Laboratory)

COPIES TO:

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- Division Chief (EES)
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- Other

CA–3 (3/76)

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

SPONSORED PROJECT TERMINATION

Date: June 10, 1980

Project Title: Hemodynamics of Normal and Diseased Carotid Arteries

Project No: E-16-D01

Project Director: Dr. D. P. Giddens

Sponsor: DHEW/PHS/National Heart, Lung and Blood Institute

Effective Termination Date: 8/31/79

Clearance of Accounting Charges: 8/31/79

Grant/Contract Closeout Actions Remaining:

None

Project Continued on E-16-D02

_ Final Invoice and Closing Documents
_ Final Fiscal Report
_ Final Report of Inventions
_ Govt. Property Inventory & Related Certificate
_ Classified Material Certificate
_ Other _____

Assigned to: Aerospace Engineering (School/Laboratory)

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CA–4 (1/79)

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Department of Health, Education, and Welfare

Grant No. 1 R01 HL22635-01

DATE OF THIS REPORTING PERIOD FROM 9/1/78 TO 8/31/79

PROJECT PERIOD FROM 9/1/78 TO 8/31/80

☐ CHECK IF FINAL REPORT

NAME AND ADDRESS OF GRANTEE INSTITUTION

Georgia Institute of Technology
Atlanta, Georgia 30332

TRANSACTION NO. (08)R1HL22635A

INSTITUTIONAL ID NO. E-16-D01

1. Expenditures of DHEW Funds for this Reporting Period

a. Personnel	$ 38,300.00	h. Alterations and renovations	
b. Consultant services	3,036.00	i. Other Retirement	1,133.74
c. Equipment	250.00		
d. Supplies	2,042.74	j. Total direct costs	45,844.00
e. Travel, domestic	1,081.52	k. Indirect costs: Rate * % ☒ S&W ☐ TDC	
f. Travel, foreign		Base $ *	28,538.00
g. Patient care costs		l. TOTAL	$ 74,382.00

2. Expenditures from Prior Periods (previously reported)	-0-
3. Cumulative Expenditures	74,382.00
4. Total Amount Awarded – Cumulatively	74,382.00
5. Unexpended Balance (Item 4 less Item 3)	
6. Unliquidated Obligations	-0-
7. Unobligated Balance (Item 5 less Item 6)	
8.a. Cost Sharing Information – Grantee Contribution This Period	3,929.77
b. % of Total Project Costs (Item 8a divided by total of Items 1 and 8a)	% 5.0
9.a. Interest/Income (enclose check)	-0-
b. Other Refundable Income (enclose check)	-0-

10. Remarks * Total Indirect Costs to be reported on SROEAS

76% x $38,300 = $29,108.00

I hereby certify that this report is true and correct to the best of my knowledge, and that all expenditures reported herein have been made in accordance with appropriate grant policies and for the purposes set forth in the application and award documents.

Dr. D. P. Giddens, Professor — 2/13/80

SIGNATURE OF INSTITUTION OFFICER — DATE

David V. Welch, Manager, Grants & Contracts Acctg. — 2/19/80

404/894-4624 — DATE

HEW-489 (REV. 10/73) **REPORT OF RESEARCH GRANT EXPENDITURES** OMB 85R0219

E-16-D01

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION
SUPPORT SERVICES DIVISION
ATLANTA, GEORGIA 30332 (404) 894-4763

18 March 1980

REPLY TO: E-16-D01

MEMORANDUM

TO: D. P. Giddens

FROM: Otis H. Rodgers
Research Reports Coordinator

SUBJECT: Record Copies of Reports for Archives

REFERENCE: Contract/Grant No. 1 R01 HL22635-01
Title: Hemodyamics of Normal and Deseades Carotid Arteries

We are not in receipt of the two record copies of the referenced report which are required for proof of performance.

If the report has been completed, please provide us with two copies for our files.

This report - i.e. Terminal Progress report is contained in the renewal application mailed out on Feb. 1, 1980 to NIH.

Attached is are two copies of that section.

D P G.

f. If the research demonstrates that significant improvements in the recognition of carotid vascular disease are afforded by flow disturbance measurement, more thorough clinical studies for further evaluation should be pursued.

Items (a) and (c) and parts of (b) and (d) were completed prior to the present grant period. Under HL 22635-01,2 we have finished (b) and are presently working on (d) and (e). The grant application presented here will propose steps to complete (d) and (e) and to begin (f).

4. Comprehensive Progress Report

a. Period

This report covers the period September 1, 1978 through December 31, 1979.

b. Summary

The following results were obtained during the above period.

1. A system for simultaneous measurement of two blood velocity components with pulsed Doppler ultrasound was designed and constructed.

2. The performance of the two-component ultrasound system with regard to its ability to measure accurately flow disturbances was compared to that of a laser Doppler anemometer in pulsatile flows of water and water/glycerin mixtures in plexiglas tubes. Agreement between the two different measurement techniques was good for flow disturbances distal to stenoses up to 75 percent reduction in area.

3. Comparison of the two-component ultrasound system with the hot film anemometer has begun. Results at this stage are encouraging but inconclusive.

4. Continued study of our data analysis methods and experiments both in vitro and in vivo have shown that recognition of flow disturbances in the form of repeatable coherent structures may be more beneficial than turbulence detection in the case of mild stenoses.

5. Collaboration with our consultant at Imperial College, Dr. R.I. Kitney, on methods to distinguish between physiologic and pathologic flow disturbances has proceeded on schedule. Dr. Kitney has suggested several additions to our data analysis scheme, and he is presently analyzing tape recordings of our in vivo experiments in dogs.

6. Detailed flow visualization and laser Doppler anemometer measurements in steady flow through a model of the human carotid bifurcation have been completed. Regions of low and high wall shear stress, flow separation and flow reversal have been identified.

c. Detailed Report

We begin by restating the Specific Aims from Section B of our existing grant.

1. In vivo experiments which measure blood velocities in the neighborhood of stenoses in the descending thoracic aortas of mongrel dogs will be performed employing simultaneous hot film anemometer and pulsed ultrasonic Doppler/phase-lock loop instrumentation for the purpose of further establishing the accuracy of the ultrasound system.

2. Measurements of blood velocity in the carotid region of human subjects will be performed with the ultrasound instrument. The purpose of these studies is to provide a fluid dynamic description of normal and pathologic flow fields in the human carotid.

3. The results of the measurements on human subjects will be compared with independent laser Doppler anemometer measurements in laboratory models of the human carotid arterial complex. No funds are being requested, however, for the actual in vitro model construction and measurements. The purpose of this phase is to determine whether detailed flow field studies in carotid models are representative of actual carotid flows. If such is the case, the laboratory models will prove extremely useful since conditions may be controlled much more easily than in human measurements.

4. It is necessary to establish methods to adequately deal with physiologic -induced disorder which may occur due to factors such as heart rate variability, respiration, and changes in stroke volume. Otherwise, physiologic flow disorder may unwittingly be interpreted as a pathologic disturbance in human measurements.

5. Finally, based upon the results of these four previous steps, the specific methods for characterizing flow disorder will be evaluated with regard to their usefulness in a noninvasive diagnostic procedure.

Progress relative to each of these specific aims will be discussed.

Specific Aim #1. At the time we wrote our original grant application for HL22636-01 we had demonstrated that phase lock loop processing of pulsed Doppler ultrasound signals gave good results for turbulence measurements in steady and pulsatile flow of water through tubes with no constrictions present. While awaiting the outcome of that application, we began a series of in vitro measurements distal to stenoses in these tubes since we anticipated proceeding with Specific Aim #1 as soon as the grant was awarded. These in vitro studies, however, showed that the measurement of a single velocity component (typically oriented at 45^{o} to the tube axis) with ultrasound would not be sufficient to give a valid comparison with hot film data recorded in the dog aorta. The reason was simple. The poststenotic flow field frequently contains nonisotropic turbulence, even along the flow centerline, in contrast to the case of flow in unconstricted tubes for which the turbulence is very nearly isotropic at the centerline. The net result of this is that a simple cos θ correction for the angle of the ultrasound beam is insufficient to describe the velocity in the axial direction. This is documented in Ref. 3. Since the objective was to eliminate as much

uncertainty as possible in the hot film/ultrasound comparison, we believed that it was appropriate to modify our ultrasound system so that axial velocity, at least at the vessel centerline, could be determined. We therefore designed and constructed a two-component pulsed Doppler (PD) ultrasound system and probe holder. This necessitated building a second single-channel PD instrument, coupling it to the same master oscillator as the original instrument, and synchronizing the transmission of pulses from each device in an alternating fashion. A schematic of the system and a sketch of the probe holder employed for animal experiments is shown in Figure 1.

The principle of operation is to transmit a pulse from one transducer and receive its echo from the desired sample volume prior to the transmission of a pulse from the second transducer. This avoids "cross-talk" between the two ultrasound beams. The velocity components u* and v* are measured at $\pm 45^{\circ}$ to the vessel axis and then rotated, assuming that flow is axisymmetric, into axial and radial components u and v. For in vitro studies the laser Doppler anemometer is employed to measure the axial component u directly while for in vivo experiments the hot film probe is placed just at the intersection of the ultrasound beams to measure u. Unfortunately, the separation of u and v components is not precise with the hot film probe since, although the probe is calibrated for the u component, it senses an undefined effect from the v component. Although this tends to cast an uncertainty upon the hot film data, it is unavoidable for the animal experiments.

Following this we began in vitro studies in poststenotic fields using steady and pulsatile flow. The sole purpose was to compare LDA and two-component pulsed Doppler (2 PD) ultrasound measurements of axial velocity, not to generate more fluid dynamic data. Since there are conflicting seeding requirements (i.e. the LDA requires small concentrations of seeding particles while the PD needs large concentrations), simultaneous laser and ultrasound measurements could not be obtained. Therefore, we attempted to repeat the same flow conditions when making comparisons.

For moderate stenoses (50 percent reduction in cross-sectional area) the agreement between laser and ultrasound measurement was excellent. This is illustrated in Figure 2 where the ensemble average axial velocity waveforms, $\langle u(t) \rangle$, and the energy spectra of the disturbance velocity are compared for the two instruments. Flow conditions approximated those we anticipated for the dog aorta. For more severe stenoses (75 percent reduction in cross-sectional area) where turbulence during the deceleration phase was much more intense, the agreement was not as good. Figure 3 gives the comparison for $\langle u(t) \rangle$ and the energy spectra. The ensemble average waveforms agree reasonably well and the coherent disturbance occurring in the acceleration phase is detected nicely by both instruments. The slightly higher values of $\langle u(t) \rangle$ which occur for the ultrasound measurement in low velocity regions of the cycle are very likely attributable to small differences in pump settings between the experiments. Comparison of the energy spectra of $u'(t)$, the axial disturbance velocity, is good for the lower frequencies; but differences appear in the high frequency region of the spectrum. We generally experienced more difficulty in maintaining "lock" with the frequency tracker for the PD than for the LDV when extremely large turbulent fluctuations were present. This may be termed a "signal dropout" problem in frequency tracking.

Generally speaking, we were pleased with the performance of the two component ultrasound system with phase-lock loop tracking for the in vitro experiments. The accuracy was very good up to turbulence levels at which signal dropout became a problem. We therefore proceeded to the hot film/ultrasound experiments in the dog aorta.

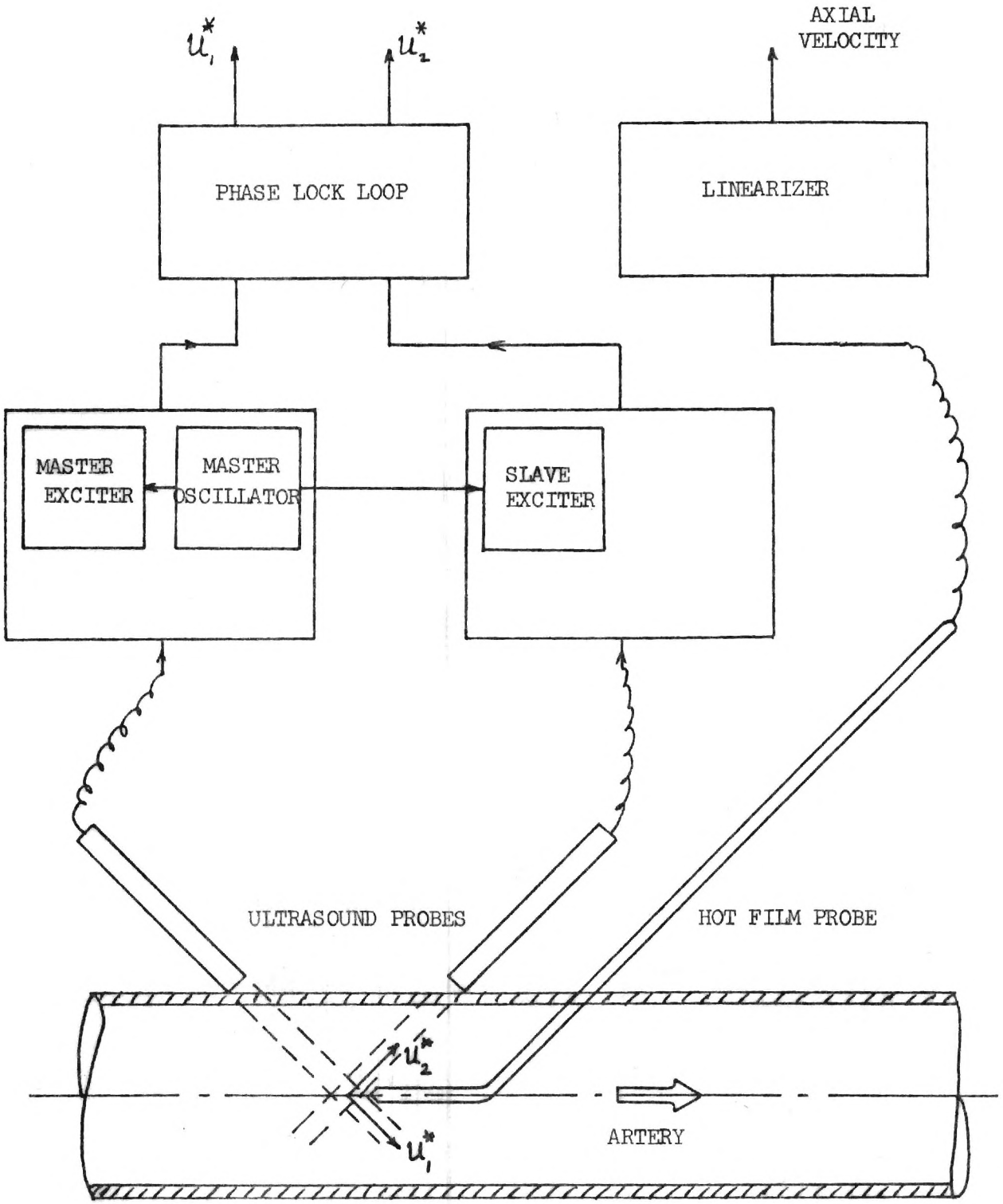


Figure 1. Schematic of two-component Doppler system and sketch of probe holder.

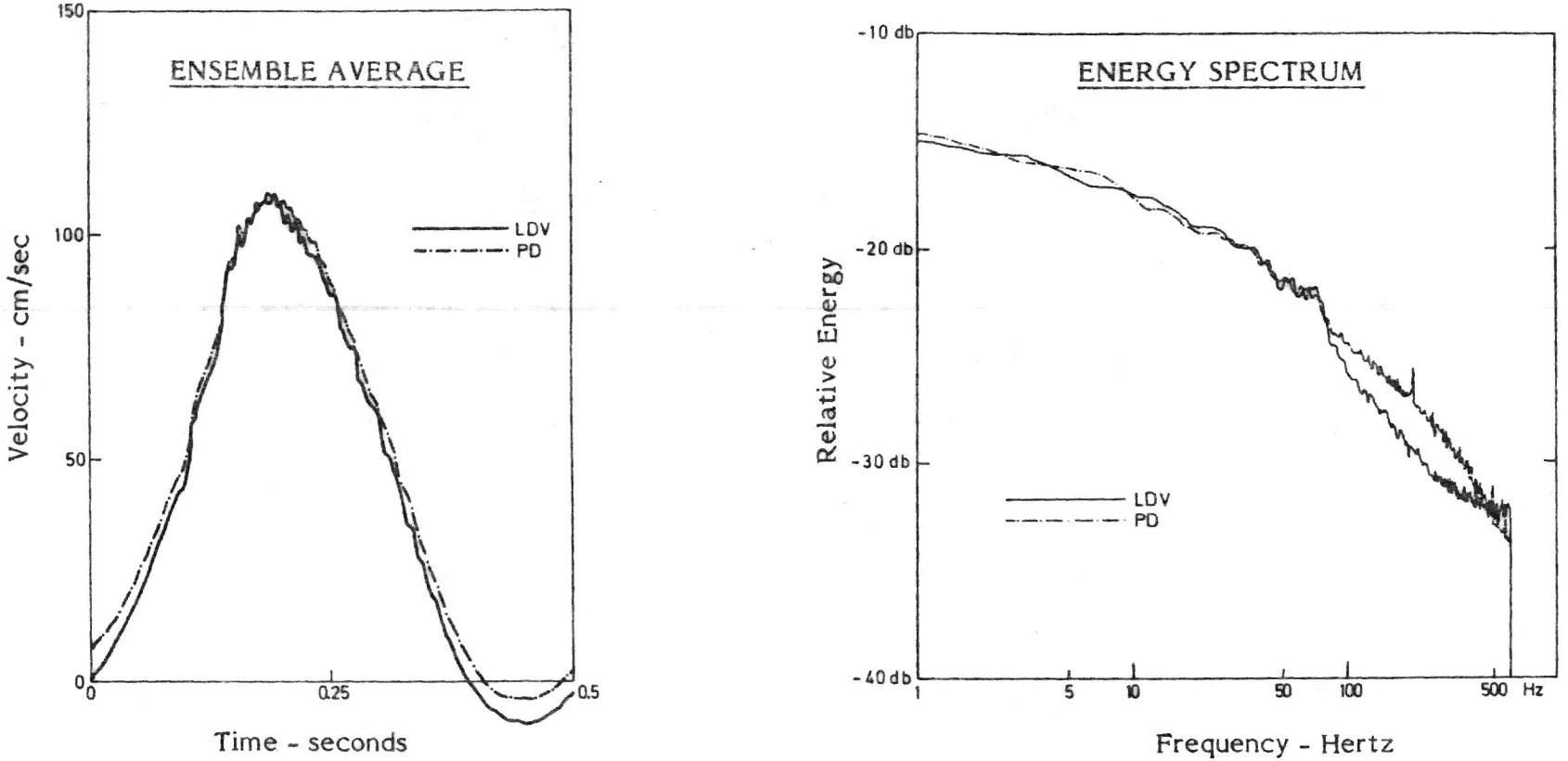
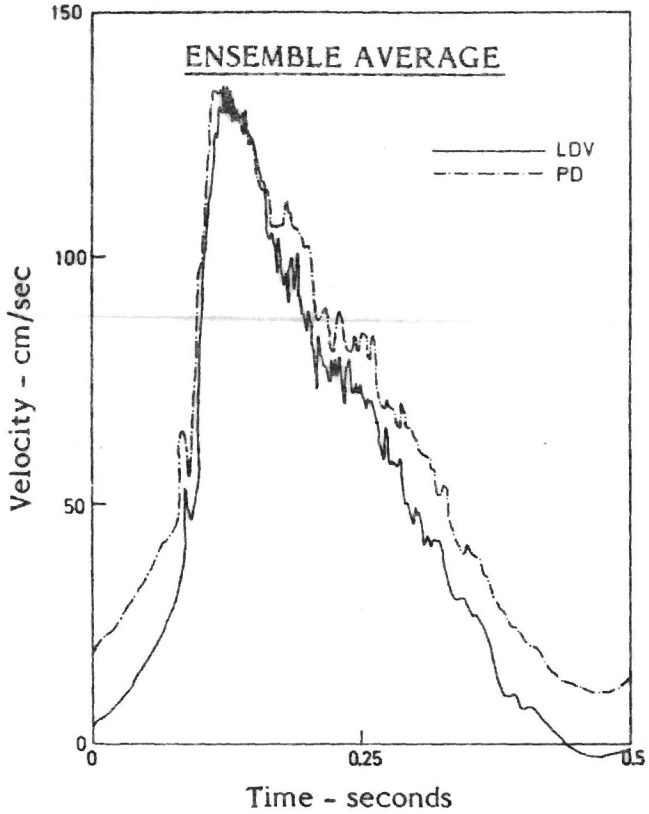


Figure 2. Comparison of LDV and PD/PLL measurements of ensemble average velocity waveform and disturbance velocity energy spectrum for 50 percent stenosis in vitro.



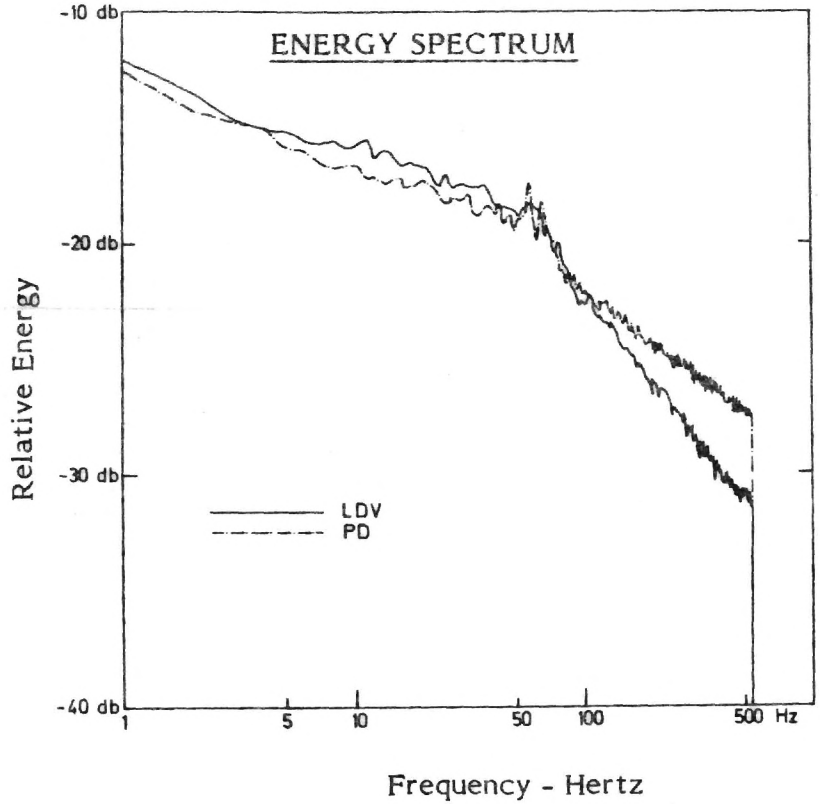


Figure 3. Comparison of LDV and PD/PLL measurements of ensemble average velocity waveform and disturbance velocity energy spectrum for 75 percent stenosis in vitro.

The objective of the hot film/2 PD experiments was to establish some level of confidence in the accuracy of the ultrasound system under in vivo conditions. This phase of the research program has proven to be extremely difficult to accomplish due to the complex nature of the experiments. Although we had performed numerous successful hot film experiments in the dog aorta prior to this grant, the addition of two ultrasound probes and the associated supplementary data to be recorded was found to be much more complicated than we envisoned. The probe holder which accommodated the hot film and two ultrasound probes was redesigned several times to allow easier and more reliable application during the surgery. The surgical procedure itself had to be modified since we were faced with the conflicting requirements of providing a large access to the aorta while attempting to maintain the animal in stable condition for long periods of time. We were plagued with several hot film probes which malfunctioned during the experiment. Finally, we experienced several difficulties with the dogs varying from a tendency to resist our efforts to stabilize cardiac output to a case of having to cancel an experiment because of a viscious animal.

We therefore have only limited reliable data at this stage of the program, and we are not satisfied with progress toward our objective. Figures 4 and 5 present two cases for which a reasonable comparison of hot film and ultrasound measurements can be made. Figure 4 gives the ensemble average waveform for one experiment where no constriction was placed about the dog aorta. The hot film measurement is approximately 20 percent lower than the ultrasound data, a difference which can easily be caused by the sensitivity of the performance of the hot film to changes in the blood temperature. The important fact is that the shapes of the waveforms are in very good agreement. The value of the dimensionless disturbance velocity, u'_{rms}/U_{peak}, averaged over the cycle is 0.03 for each measurement. Figure 5 gives the ensemble average waveform for a case of 75 percent occlusion, the point of measurement being 3.5 diameters distal to the stenosis and at the vessel axis. Again, the general shapes of the ensemble average waveforms agree well with the hot film data being approximately 20% lower. The average values of u'_{rms}/U_{peak} were 0.11 and 0.13, respectively, for the hot film and PD measurements.

Although, as illustrated by the Figures 4 and 5, we have several cases recorded for which agreement between the two measurement techniques is good, we have numerous cases for which comparisons are poor. This may be due to several reasons:

i. The hot film probe is not properly aligned with respect to the ultrasound sampling volume.

ii. The output of the hot film probe is extremely sensitive to the overheat ratio which, in turn, is sensitive to small changes in blood temperature.

iii. There are often small blood clots occurring on the hot film probe surface which affect its response.

iv. For intense turbulence the hot film probe output is affected by transverse velocity fluctuations so that the measurement may not be accurately representative of the axial component.

v. For intense turbulence the phase lock loop may "lose track" and suffer signal dropout.

vi. There is a tendency for the ultrasound data to be somewhat "noisier" than the hot film data.

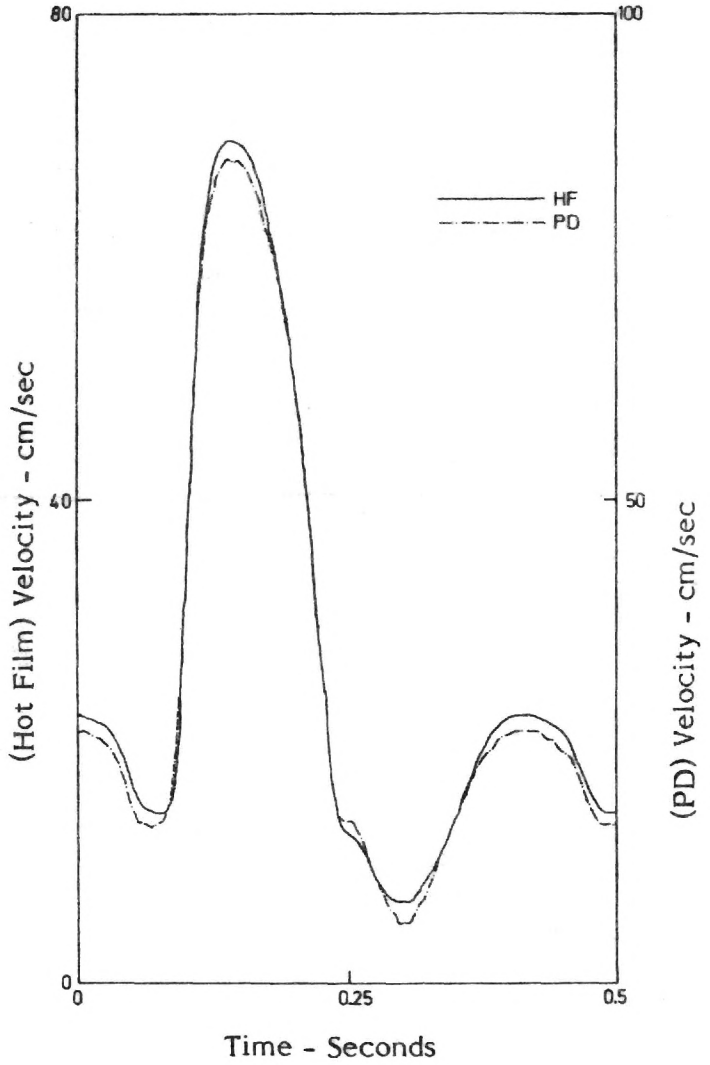


Figure 4. Comparison of hot film and PD/PLL Measurements of ensemble average velocity waveform in the unconstricted dog aorta.

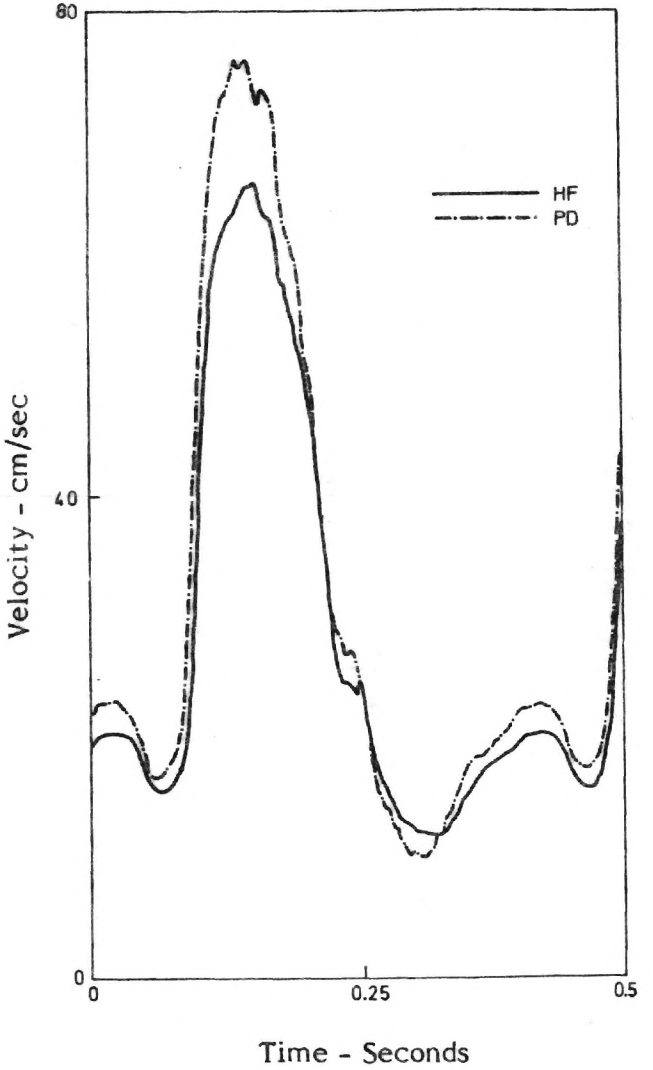


Figure 5. Comparison of hot film and PD/PLL measurements of ensemble average velocity waveform in the dog aorta, 3.5 diameters distal to a 75 percent stenosis.

On the positive side, however, we do see good agreement for several cases which, given the nature of the signals involved, cannot be fortuitous. We intend to continue our efforts to clarify these comparisons during the present grant period.

Specific Aim #2. To date we have designed several and constructed one ultrasound probe holders to be employed for two-component velocity measurements on the carotid arteries of human subjects undergoing endarterectomy. The design requirements are much more stringent for the human studies since we must accommodate our probes to the needs of the vascular surgeon, thus requiring miniturization of the probe-holding devices. We recently tested one such probe holder in an animal experiment and performance was very good. We should be able to move directly to measurements of velocity in the exposed carotid artery during endarterectomy so that detailed data on diseased cases may be gathered, following the protocol outlined in our previous grant application.

Specific Aim #3. We have always insisted on coupling model studies in vitro with our in vivo work. When our previous NIH grant proposal was written, we were in the process of establishing a model of the human carotid arteries with the view of performing laser Doppler anemometer measurements of the velocity field. This work was begun with funding from an NSF grant. During the course of that study the NSF grant expired, and we continued the experiments with funds from HL 22635 to support the graduate student involved and necessary supplies. We have recently completed steady flow measurements in this model and report briefly here on significant results. Details are documented in a Ph.D. thesis by Dr. K. Balasubramanian and a preliminary paper (see Section A.4.d of this application for these references).

The primary objective of this phase of research is to provide accurate and detailed fluid dynamic data under carefully controlled laboratory conditions which can be employed to aid our understanding of in vivo velocity measurements in the human carotid arteries, the latter data being much less detailed with poorer resolution and obtained under conditions which are much more difficult to control. This research to date has been composed of three phases: (i) design and construction of a model representative of the carotid bifurcation in humans; (ii) flow visualization with hydrogen bubble and dye injection techniques under steady state conditions; and (iii) measurements of the velocity field with a laser Doppler anemometer for steady flow.

We have gone to great lengths to configure the bifurcation model to be a reasonable representation of the human carotid complex. Biplanar angiograms from subjects ranging from infancy to 70 years of age were employed. Geometric measurements at 15 different sites were averaged to arrive at the average configuration. As expected, wide variations in geometry were encountered, and we do not portray our model as a "typical" carotid bifurcation, but rather a "representative" one. Figure 6 and Table 1 give the final results of the configuration phase of the study. Full details are to be found in Dr. Balasubramanian's thesis (Ref. 9). The model is of plexiglas, and therefore rigid, to enable use of the LDA. We expect that effects on the flow field will be dominated by the geometrical shape of the bifurcation and pulsatility of the flow rather than by the viscoelasticity of the wall. Additionally, since the constituitive equations of the carotid arterial wall are not really completely known, it is not a straightforward matter to define a material which properly models the viscoelastic behavior and is transparent to light. For those reasons we intend to continue use of the rigid models for the studies proposed in this renewal application while keeping in mind the possibility of eventual extension to viscoelastic models.

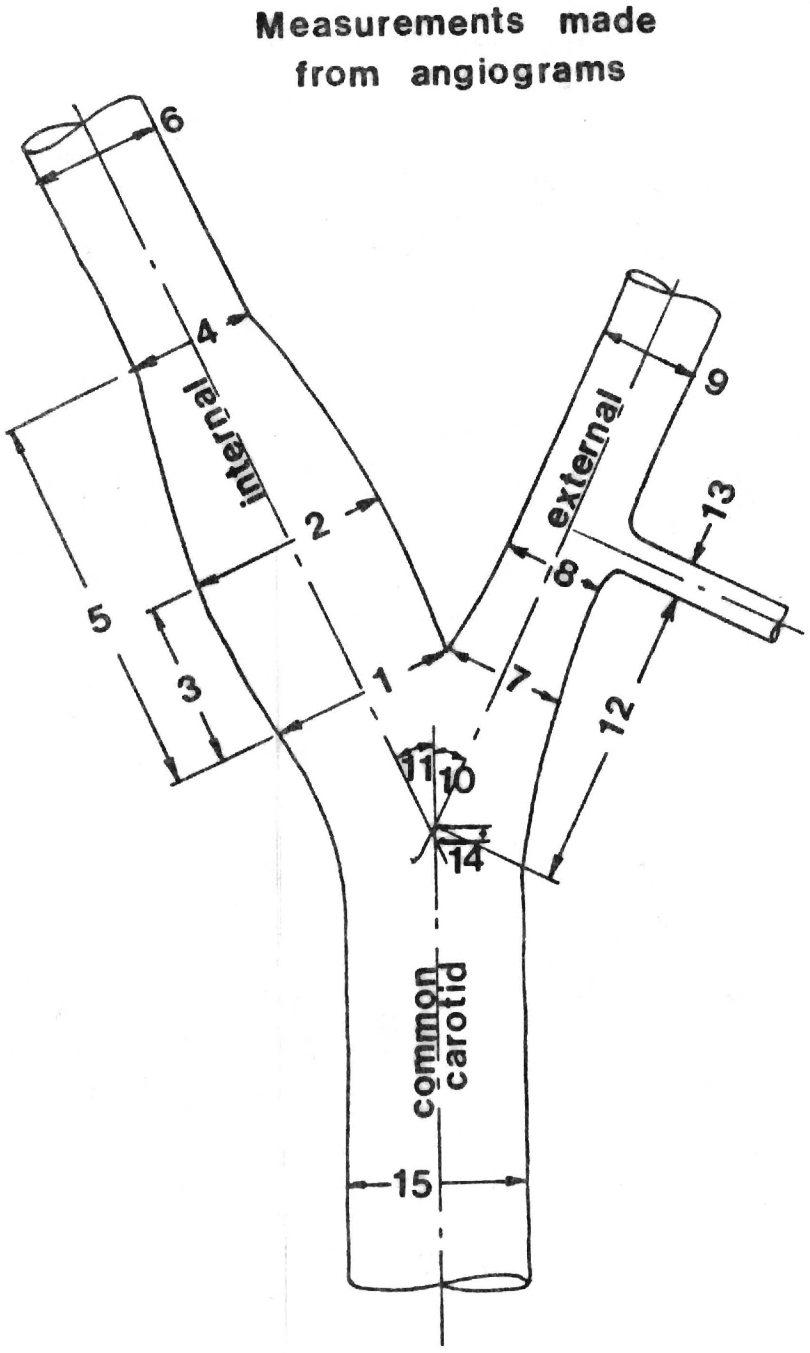


Figure 6. Geometry of the carotid model.

Table 1. Variation of Important Parameters at the Human Carotid Bifurcation with Age

Location	Up to 3 Yrs.	3-11 Yrs.	11-18 Yrs.	Adults
Percentage of angiograms with definite sinus	6%	59%	92%	-
Diameter of common carotid artery*	1.00	1.00	1.00	1.00
Maximum sinus diameter*	.84	.96	.97	1.11
Diameter of internal* carotid artery distal to sinus	.84	.77	.79	.69
Diameter of external* carotid artery	.70	.60	.58	.58
Projected angle between external and common carotids (lateral view only)	20.92°	15.67°	12.87°	15.77°
Projected angle between internal and common carotids (lateral views only)	42.50°	26.88°	13.45°	23.36°

*Numbers shown are made dimensionless by the diameter of the common carotid artery.

Although steady flow was employed in the first phase of the study, all other flow conditions were prescribed to be representative of values found in human subjects. For example, a representative flow rate in the common carotid artery for healthy adults is 500 ml/min with a 70:30 flow division ratio for the internal: external branches. Data in the literature suggest a common carotid diameter of 7 to 8 mm, and the high shear rate value of blood viscosity is approximately 0.035 cm^2/sec (at the shear rates encountered in the carotid arteries a Newtonian approximation for blood viscosity is quite adequate for this study). Taking 8 mm as the diameter along with the above values for mean flow rate and viscosity gives a mean Reynolds number of approximately 400. If Reynolds number is based upon the peak velocity during the cycle, the value is approximately 1200. Therefore, in our studies we examined flows at Reynolds numbers of 400, 800, 1200 and 1400 and flow division ratios of 60:40, 70:30 and 80:20. The model was scaled upward in size to allow better resolution for the LDA measurements and the fluid employed was a water/glycerin mixture whose viscosity was adjusted, along with pump output, to give the proper Reynolds number.

Hydrogen bubbles generated from a 50 μm wire and dye injected by a catheter were employed to visualize the flow. Figures 7 and 8 illustrate some of the phenomena present. (Since the H_2 bubbles tended to cling to plexiglas, the flow visualization was accomplished in a glass-blown model which closely approximated the geometry of Figure 6. The LDA measurements were obtained in the machined plexiglas model.) For all conditions studied there was flow separation, reversal and strong helical patterns in the carotid sinus. Figure 7 illustrates the separated flow phenomenon with hydrogen bubbles. The region of separation is complex, however, as shown in Figure 8. Strong three-dimensional flow is evidenced by the pair of counter-rotating helices, visualized by dye. Hundreds of photographs were made under a variety of flow conditions and many more examples are given in Ref. 9. We summarize here the results of the flow visualization.

- Flow separation followed by flow reversal occurs at the outer corner of the common-internal junction under all flow conditions investigated.
- At the outer corner of the common-external junction, separation is observed only when the flow rate through the external carotid is very low -- 20% or less.
- The points of separation in the plane of bifurcation move with changes in flow division and upstream Reynolds number.
- Strong secondary flows are present in both branches of the bifurcation.
- At high Reynolds numbers oscillations are observed in the sinus even though the overall flow field is steady.
- The shear stress along the inner walls is quite high compared to that near the outer corners.
- There is a band of low shear stress in the common carotid very close to, but upstream of, the branching.

Following the flow visualization studies, measurements of velocity were taken with a single-component LDA system. Figure 9 is a photograph of the model and laser system. Again, a large quantity of data were taken and documented in Ref. 9. We present in Figure 10 an example of velocity profiles measured in the plane of the bifurcation for a

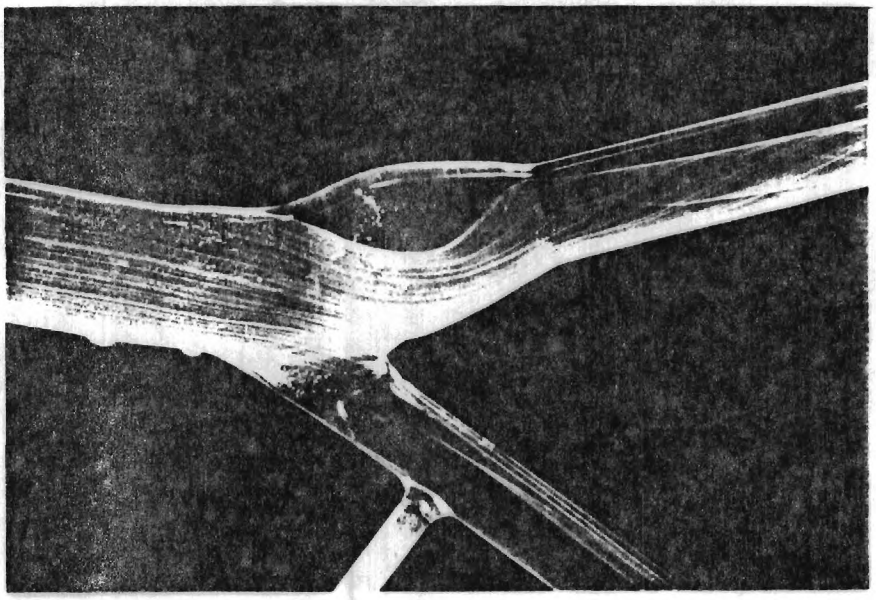


Figure 7. Flow separation near the common-internal corner as visualized by hydrogen bubbles. (Re = 400, 70:30 flow division, cathode wire in plane of bifurcation.)

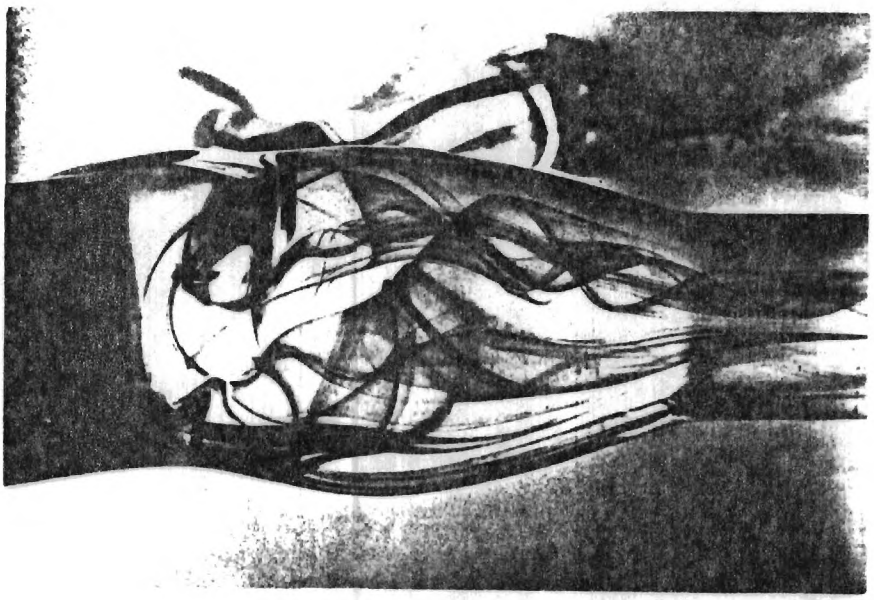


Figure 8. Intermixing of counter-rotating helices within the carotid sinus. (Re = 1400, 70:30 flow division.)

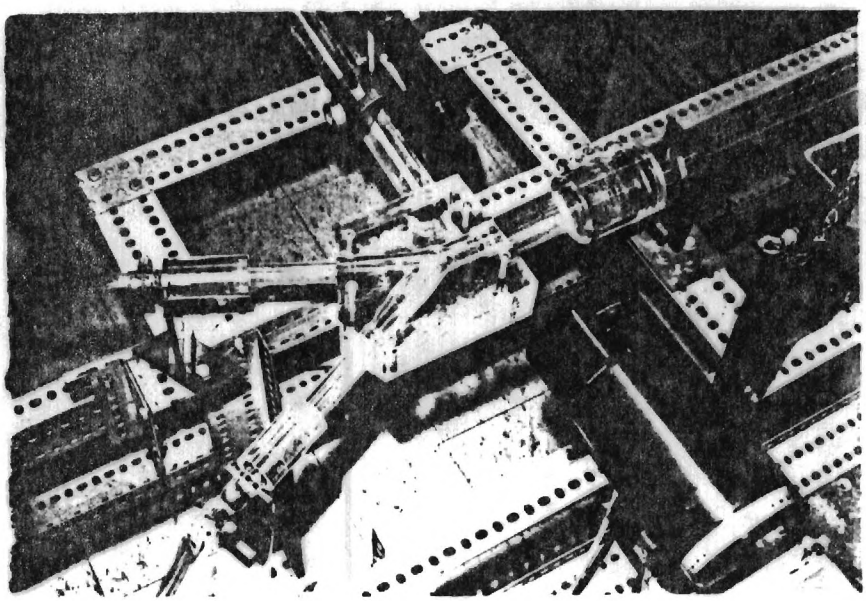


Figure 9. Photograph of carotid bifurcation model and laser Doppler system.

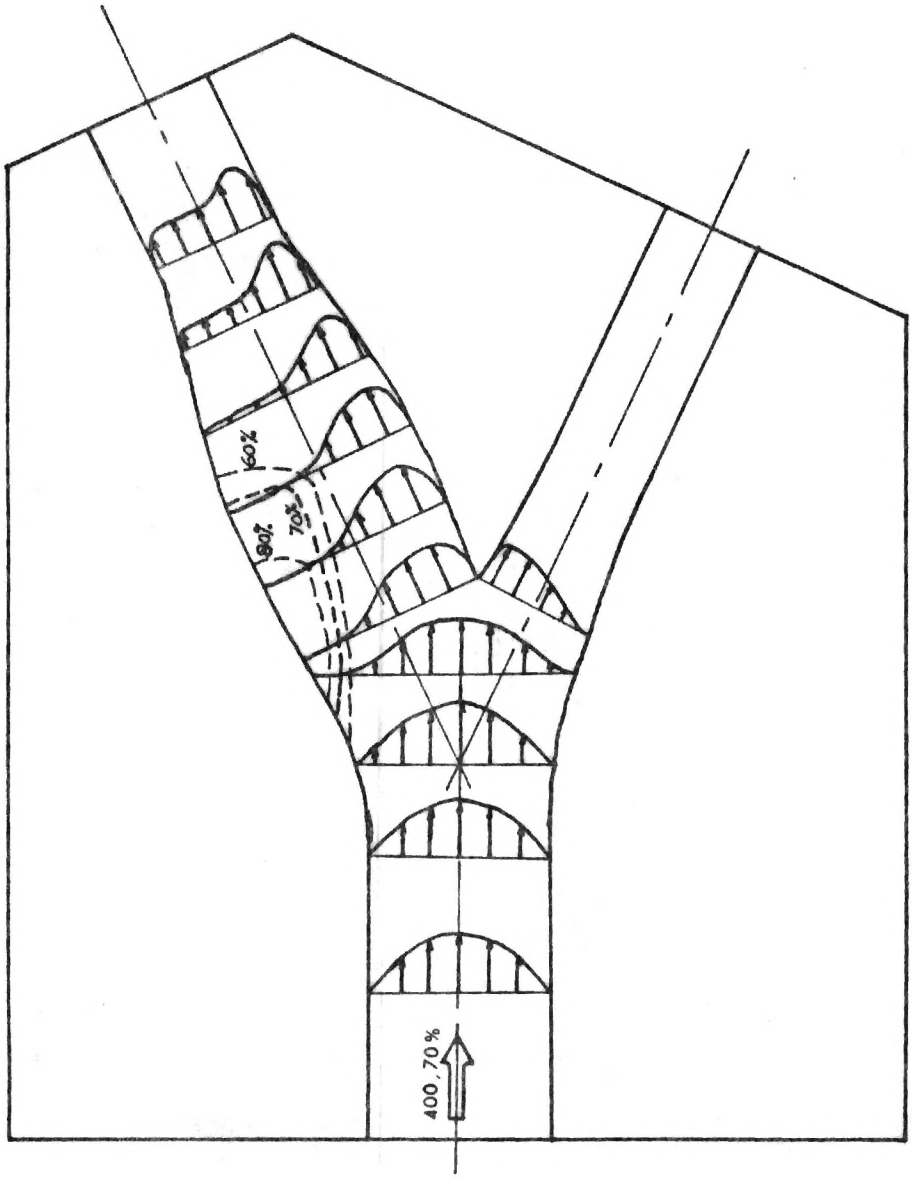


Figure 10. Velocity profiles in the plane of bifurcation. Re = 400 and 70:30 flow division. Dashed lines in the sinus indicate extent of reverse flow region for flow division ratios of 60:40, 70:30 and 80:20.

Reynolds number of 400 and flow division ratio of 70:30. The velocity profiles in the branches are strongly skewed, and the region near the flow divider is subjected to a relatively high wall shear stress while the separated flow region is one of very low wall shear stress. Flow was remarkably laminar under all conditions except Re = 1400, for which transient instabilities occurred. A list of results from the LDA measurements follows:

- Flow in the parent vessel is virtually unaffected by the bifurcation.
- In the plane of bifurcation, the point of separation near the carotid sinus moves upstream with increasing Reynolds number and decreasing flow through the internal carotid. However, the movement is quite small.
- The region of reversed flow in the sinus grows in size with increasing Reynolds number and decreasing flow through the internal carotid.
- In the sinus, the axial velocity profile in the plane of bifurcation is skewed towards the inner wall.
- Axial and tangential velocity profiles along diameters normal to the plane of bifurcation demonstrate peaks near the artery walls.
- The shear stress along the inner wall of the sinus can be as high as 125 dynes/cm^2 at an upstream Reynolds number of 1200, compared to about 5 dynes/cm^2 in the reversed flow zone.
- The shear stress along the side walls of the sinus is approximately 50 dynes/cm^2 when the Reynolds number is 1200.
- The direction of the shear stress along the side walls of the internal carotid varies considerably with changes in Reynolds number.
- In the internal carotid artery, immediately downstream of the sinus, the peak velocities are higher than in the sinus.
- The wall shear stress in the internal carotid artery, immediately downstream of the sinus, is of the same order as that along the inner wall of the sinus.
- At the outer corner of the common-external junction, the shear stress decreases with increasing Reynolds number and a reversed flow zone is observed only at very low flow rates through the external carotid.

The relevance of this study to disease detection will be discussed in Section C, Methods of Procedure.

Specific Aim #4. The development of techniques to deal with the separation of physiologic from pathologic disturbances involved collaboration with Dr. R.I. Kitney of the Engineering in Medicine Laboratory, Imperial College. The following progress has been made toward achieving Specific Aim #4.

i. In May 1979 Dr. Kitney visited our laboratory for the purpose of thoroughly understanding our goals and experimental methods. We illustrated our velocity measurement techniques, methods of data analysis, and held an experiment to measure velocity in the dog aorta with hot film and ultrasound. Dr. Kitney discussed effects of respiration, blood pressure and thermoregulation upon heart rate variability and made several tentative suggestions regarding the data analysis.

ii. Upon returning to Imperial College Dr. Kitney began developing his own computer programs to reproduce our current methods of data analysis to serve as a foundation for examining the effects of biologic variability. We sent an FM tape recording of some of our previous data which he was to subject to flow disturbance analysis.

iii. In August 1979 Dr. Giddens visited Imperial College for one week. Drs. Kitney and Giddens worked on checking out the computer programs at Imperial College. Additionally, quite by chance, Dr. Giddens observed that one of Dr. Kitney's graduate students was working with hot film measurements of velocity in the aorta, obtained from catheterization of human subjects in the clinical laboratories of Dr. Alastair McDonald, Cardiology Department of London Hospital. The data from some of the patients appeared to have flow disturbances during the deceleration phase of the cycle, and it was decided to apply flow disturbance analysis to Dr. McDonald's data in the future.

iv. Subsequent to the visit in August Dr. Kitney has completed the basic computer programs and sent to our laboratories the results of this analysis on our previous data for comparison. We are now sending him a copy of a recent experiment involving ultrasound data for him to analyze.

v. We have prepared an abstract of a paper to be presented at the Bio-Eng 80 conference in London in March 1980 and are working on the data analysis for that presentation.

We are very pleased with the progress made in this phase of the research program. Dr. Kitney has taken a much more active role in the project than we envisioned. We anticipated using him as a consultant to make suggestions for us to carry out. Because of his interest in the project he has developed his own computer programs and will be performing a significant amount of data analysis himself. A further unexpected benefit is that our ideas of flow disturbance analysis may prove useful to Drs. Kitney and McDonald in their research on velocity measurements with patients suspected of having aortic valve and aortic stenosis problems.

Specific Aim #5. Although we have not gathered sufficient data to be able to claim great progress towards achieving this specific aim, one potentially significant result appears to be emerging: coherent disturbances may be a more important factor than turbulence in the detection of early disease. This suggestion is based upon in vitro experiments with constrictions in a straight tube and upon poststenotic velocity measurements in the dog aorta. We do not yet have any data related to this aspect from human carotid arteries.

An example of a poststenotic coherent structure is given in Figure 11. This figure gives results of LDA velocity measurements in vitro at several axial positions distal to a stenosis of 25 percent reduction in cross-sectional area. The ensemble average velocity waveform $\langle u(t) \rangle = U(t)$, obtained by averaging flow for 100 cycles, is graphed along with the mean

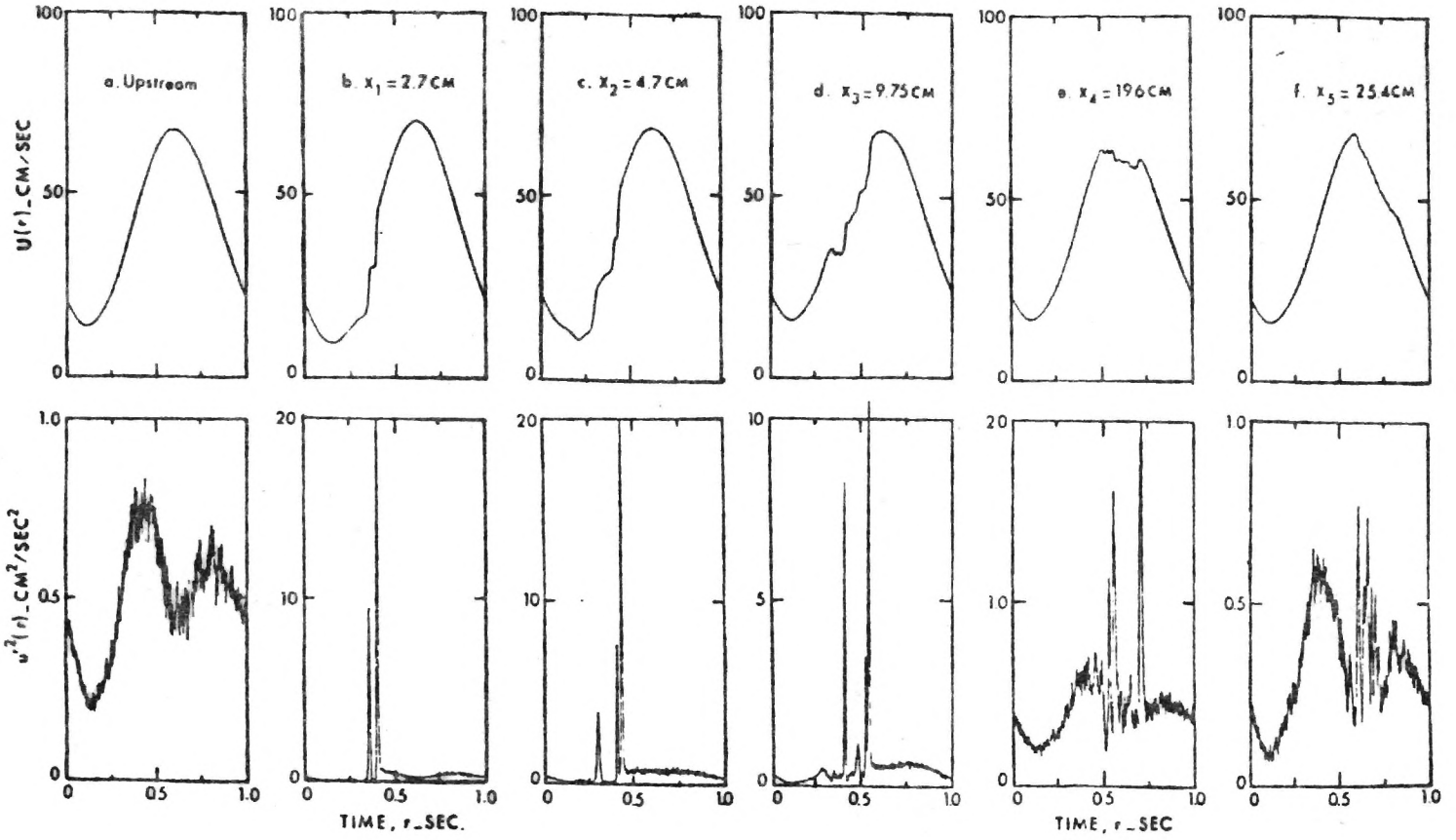


Figure 11. Ensemble average and disturbance velocities at various axial locations distal to a 25 percent stenosis in vitro.

square of the disturbance velocity defined by $u'^2(t) = \langle u(t) - U(t) \rangle^2$ and also averaged over 100 cycles. The effect of ensemble averaging is to remove any random features of the flow while retaining coherent or repeatable features. It can be seen that the U(t) waveforms contain clearly repeatable features which propagate very far downstream. The u'^2 graphs show that the random disturbance velocity is quite small except for sharp peaks which serve to mark the passage of the coherent structures. These spikes arise because the structures are not precisely repeatable. For this particular case no turbulence is present - the only flow disturbances are coherent ones.

Additional results are to be found in Ref. 10 and in a manuscript which is under review. The in vitro measurements for 50 and 75 percent stenoses produced three types of flow disturbance: coherent structures, shear layer instabilities, and turbulence. As indicated in Ref. 2 poststenotic coherent structures and turbulence have been observed in the dog aorta, and our current animal studies with hot film and ultrasound continue to demonstrate this. However, it was not until we performed the detailed and well-controlled in vitro experiments that we fully appreciated the potential of the coherent structures in detecting mild constrictions.

An additional factor of importance is this: the frequency response required to measure the coherent disturbances is not as great as that required to measure turbulence accurately. Thus, although high frequency response of ultrasound measurements is a difficult problem, it is not as critical for coherent structure detection as it is for turbulence.

d. Publications

1. Ph.D. Theses supported in part under this grant.

   - "The Role of Flow Disorder in the Noninvasive Detection of Atherosclerosis" by A.M.A. Khalifa

   - "An Experimental Investigation of Steady Flow at an Arterial Bifurcation" by K. Balasubramanian

2. Papers Published

   - "Steady Flow at the Carotid Bifurcation" by K. Balasubramanian, D.P. Giddens, and R.F. Mabon. To appear in the Proceedings of the Second Mid-Atlantic Conference in Bio-Fluid Mechanics, Plenum Press, May 1980.

3. Manuscripts Completed and Under Review

   - "Characterization and Evolution of Poststenotic Flow Disturbances" by A.M.A. Khalifa and D.P. Giddens, submitted to Journal of Biomechanics.

4. Papers Presented

   - "Hemodynamic Disorder and its Noninvasive Measurement" by D.P. Giddens, 31st ACEMB, October 1978 (invited).

   - "Hemodynamics of the Carotid Artery", by K. Balasubramanian, R.F. Mabon and D.P. Giddens, 72nd Annual AICHE Meeting, November 1979.

- "Doppler Ultrasound Measurement of Two Turbulence Components", by A.M.A. Khalifa, R.F. Mabon and D.P. Giddens, 32nd ACEMB, October 1979.

- "Evolution of Disorder in Poststenotic Flows" by A.M.A. Khalifa, R.F. Mabon and D.P. Giddens, 32nd ACEMB, October 1979.

- "Flow Disturbance Analysis of Aortic Velocity Waveforms" by R.I. Kitney, D.P. Giddens and R.F. Mabon, to be presented at Bio-Eng 80 Conference on Blood Flow, London, March 1980.

- "Flow Disturbance Measurement with Doppler Ultrasound" by D.P. Giddens, R.F. Mabon and A.M.A. Khalifa to be presented at 15th Annual AAMI Meeting, April 1980 (invited).

- "Steady Flow at the Carotid Bifurcation" by K. Balasubramanian, D.P. Giddens and R.F. Mabon, Second Mid-Atlantic Conference in Bio-Fluid Mechanics, May 1980.

e. Staffing

The following professional personnel worked on this project to date:

i. Don P. Giddens, Ph.D., Professor, September 1, 1978 to present.

ii. Robert F. Mabon, M.D., Professor and Neurosurgeon, September 1, 1978 to present.

iii. A.M.A. Khalifa, Ph.D., Postdoctoral Fellow, December 1, 1978 to January 23, 1980.

iv. R.I. Kitney, Ph.D., Lecturer, Imperial College Consultant during grant period.